

REMARKS

In view of the preceding amendments and the comments which follow, amendment and reconsideration of the Office Action of May 31, 2006 is respectfully requested by Applicants. This response is being submitted along with Applicants' Request for Continued Examination.

Claim 4 has been cancelled. Claims 1, 7, 9-11, and 17 have been amended. Claim 18 is new. In claims 1 and 17, the recitation "distinct" has been eliminated, and claim 7 has been amended for clarity. In claims 9-11, a period has been added at the end of the claim. Support for new claim 18 is found in claim 1 as originally filed and in the specification on page 10, lines 29-32. No new matter has been added.

Claims 1-3 and 5-18 are currently pending for examination.

Rejections under 35 USC §112

Claims 1-17 have been rejected under 35 USC §112, first paragraph, for their recitation of "a separate and distinct semipermeable membrane". The examiner argues that, while the figures show separate pieces of membranes attached to the wells, there is no indication of any distinctness between them.

Applicants have now amended claims 1 and 17 to remove the recitation "and distinct". They respectfully request the examiner's reconsideration of the rejection.

Claim 7 has been rejected under 35 USC §112, second paragraph, for being indefinite in the limitation recited for the fixing parts.

Applicants have now amended claim 7 to clarify the recitation and limitation. They respectfully request the examiner's reconsideration of the rejection.

Rejection under 35 USC §103

Claims 1-17 have been rejected under 35 USC §103 (a) as being unpatentable over Schels et al., U.S. Patent No. 6,670,173 (hereinafter "Schels") in view of Manns, U.S. 5,047,215 (hereinafter "Manns") and/or Wolf et al, U.S. 5,462,874 (hereinafter "Wolf"). The examiner states that Schels teaches a microdialysis device having a sample chamber (12) and dialysate chamber (10) separated by a membrane (7). The periphery of the membrane is fixed in compression between the groove on the circumferential ring part of the chamber and the ridge on the bottom face of the sample chamber wall (see Fig. 5 and also Figs. 2-4). The sample chamber is open only to the dialysate chamber via the membrane having individual

dialysate chambers for the sample chamber. The membrane is cellulose acetate. The teaching of the Schels reference differs from the instant claims in the plurality of the sample chambers, common dialysate chamber, dimensions such as wall thickness, the 3 mm difference in the diameter between the sample chamber and the circumferential sidewall of the sample chamber, the membrane area, spacing of the sample chambers, and the number of sample chambers in the device. The examiner states that the Manns reference teaches 96-well multiwell structure (Fig. 1) with a common dialysate chamber, cellulosic membrane (col. 4, l. 29-35), membrane clamped in groove and rib (see figures), and membrane area is about 32 sq. mm (col. 1, l. 15-20). The examiner argues that it would be obvious to one of ordinary skill in the art at the time of the invention to use the teaching of Manns in the teaching of Schels for having a multiwell device for simultaneously handling multiple samples as taught by Manns for bioreactions as taught by Schels. Such multiwell plates are also well known in the art as taught by Manns.

With regard to Wolf, the examiner states that Wolf also teaches such multiwell plates for dialysis, wherein the multiwell plates are removable from the dialysate chamber (Figs. 3 and 5), with single dialysate chamber or separate dialysate chamber for each well, and separate membrane pieces for each well. The examiner argues that it would be obvious to one of ordinary skill in the art at the time of the invention to use the teaching of Wolf in the teaching of Schels for a multi-well dialysate chamber as taught by Wolf for the advantages taught by Wolf (abstract and col. 4, l. 58 – col. 5, l. 12).

The examiner argues that dimensional differences such as the 3 mm diameter difference or shape such as the conical bottom of the fixing part are not patentable unless applicant can show with evidence of unobviousness. For support, the examiner cites *Gardner v. TEC Systems, Inc.*, Fed. Cir. 1984, and the examiner states that the Federal Circuit held that, where the only difference between the prior art and the claims was a recitation of relative dimensions of the claimed device and a device having the claimed relative dimensions would not perform differently than the prior art device, the claimed device was not patentably distinct from the prior art device.

Applicants traverse and argue that the examiner's case for *prima facie* obviousness has not been made. The Schels, Manns, and Wolf references references simply fail to teach or suggest a multi-well device comprising individual semi-permeable membranes fixed to each well of a multi-well plate by the use of a ring that frictionally engages the side wall of the sample well. More particularly, Manns teaches a multi-well plate in combination with a semi-permeable membrane, but the reference fails to teach or suggest individualized membranes fixed to each well. This difference is significant because only in the latter case can each sample well be placed in contact with an individual dialysate chamber. The newly cited Wolf reference does teach individual membranes fixed to each well of a multi-well plate, but this

reference teaches sealing by "adhesives bonding, heat sealing, ultrasonic welding and gasket compression seals" (column 12, lines 61-67). As described in the background section of Applicants' specification, those sealing methods have proven to be inadequate. Wolf fails to teach or suggest the sealing ring that is claimed as part of the present device. Lastly Schels also fails to teach or suggest the present invention. As noted in Applicants' response of May 19, 2006, Schels is directed to a single "bioreaction module" as stated in the title of that patent. The examiner's blanket statement that the Schels device could be converted to a multi-well format ignores the space constraints and design limitations that are caused by such a modification. Applicants' claimed device allows for individual membranes to cover each well of a multi-well apparatus using a fixing ring wherein the space between wells is limited.

Applicants wish to point out and distinguish (a) the fixation of the fixing part to the circumferential side walls of the sample chambers, and (b) the fixation of the membranes to the chamber walls in a liquid tight manner. The frictional engagement refers to (a). Nothing even remotely similar is disclosed in Schels. Schels has no fixing part comprising an annular wall extending from the perimeter of the ring-shaped portion and cooperating in frictional engagement with circumferential side walls of the sample chambers. The parts clamping the membranes in the embodiments of Figures 1 to 4 of Schels are the chamber elements 3, 4, and 5. The connection of these elements is described in column 5, lines 6 to 14. Nothing disclosed therein is similar to frictional engagement, let alone engagement between an inwardly oriented annular wall of a ring and a circumferential side wall of a chamber. Rather, Schels emphasizes the importance of a sturdy and stiff connection. Thus, if anything, Schels teaches away from the present invention.

With respect to the embodiment of Figure 5 of Schels, a press fit is used to connect chamber elements 3 and 5, as described in column 6, lines 42 to 47. This could possibly be interpreted as "frictional engagement". However, with respect to this embodiment, an additional distinction is provided by the pins 36 of Schels. Regarding the fact that Schels do not show pins in the embodiment of Figures 1 to 4, Applicants point out that, by stating that use of such pins is a preferred embodiment, Schels emphasize the difficulties to correctly position a membrane in the given situation. This must be even more difficult when the dimensions are significantly smaller as in the claimed device. The dual function of the pins taught by Schels also needs to be emphasized. As taught in column 6, lines 32-36, Schels requires the use of pins for both centering and fixing.

The examiner has cited Gardner v. TEC Systems, Inc. for the proposition that "Dimensional differences such as the 3 mm diameter difference, or shape such as the conical bottom of the fixing part are not patentable unless applicant can show with evidence of unobviousness." The examiner's statement

is a mischaracterization of the holding in Gardner v. TEC Systems, Inc. First, Gardner v. TEC Systems, Inc. makes no reference to the shape of a device relative to patentability. In fact, the Federal Circuit has held that when shape is novel and serves a purpose in a manner not obvious from the prior art, it can lend patentability to a claimed product (*In re Hofmann*, 95 F.2d 257 (CCPA 1938)). The examiner has failed to cite any rationale regarding why Applicants' shape modification is obvious, and it is the examiner's burden to establish a case of obviousness before applicants are required to present evidence of nonobviousness.

In addition, regarding differences between the prior art and the claims that relate to relative dimensions, Gardner v. TEC Systems, Inc. did not hold per se that such differences are not patentable, but as noted by the examiner in *In re Dailey*, the relevant question is whether such changes in dimension have significance to the claimed invention. The court in Gardner v. TEC Systems, Inc. stressed that "the dimensional limitations of claim 1 are no more than 'window dressing'" (at page 1346 of Gardner v. TEC Systems, Inc.), and that the limitations were a verbal difference only. However in the present invention, the differences between the claimed invention and the prior art represent substantive differences. The size of the fixing ring allows it to function in a multi-well setting wherein space between the individual well walls is limited. Furthermore, as disclosed in the specification, the conical shape of the inner wall of the fixing ring advantageously optimizes the size of the exchange opening of the exchange surface (see page 11, lines 4-13, of the specification). Thus these "dimensional differences" are components of the device that allow the device to function, and are not merely superficial changes relative to the prior art.

Nor are the differences between the prior art and the presently claimed invention taught or suggested by the combined teachings of the Schels, Manns, and Wolf references. As noted above, the presently claimed invention is directed to a device comprising multiple sample wells wherein each sample well has a separate semipermeable membrane fixed to the well through the use of a fixing ring. The only reference that teaches an embodiment that uses a ring as a component for holding the membrane in place (Schels) teaches that fixing pins must also be used in such an embodiment. The examiner contends that Schels can be used without the disclosed pins, stating that the pins were only disclosed for "centering" the membrane and that Figs. 3 and 4 do not include such pins. Applicants respectfully submit that the examiner has mischaracterized the teaching of Schels. First of all, the embodiment of Fig. 5 is the only embodiment shown within Schels that uses a ring that frictionally engages the side walls of the sample vessel to assist in holding the semipermeable membrane in place. As noted at column 5, lines 6-8, "chamber elements 3, 4, 5 can be connected by conventional means used in plastic engineering, e.g., by bolting, gluing or as a plastic plug connection." Thus in the embodiments represented by Figs. 3 and 4, Schels taught that pins were not necessary, presumably because fixing means other than friction

engagement were used. However for the embodiment of Fig. 5, "in order to center and fix the membrane 7, the embodiment shown provides for a plurality (for example six) of pins 36 distributed about the periphery of and molded onto one of the chamber elements" (column 6, lines 32-35). Accordingly, an objective reading of Schels indicates that such pins provide a necessary function in fixing the membrane in place. There is nothing in any of the cited references to suggest that fixing rings having small enough dimensions to be compatible with a multi-well device could be used to fix semipermeable membranes on each well using only frictional engagement. Thus the examiner has failed to establish a *prima facie* case of obviousness.

With regard to new claim 18, which specifies that the membrane is held in place solely by the frictional engagement of the annular wall of the fixing ring with the circumferential side walls, Applicants argue that none of the cited references teach such a device. Schels requires the use of pins for centering and fixing. Wolf fails to even suggest that frictional engagement could be used to hold the individual membranes in place. Absent Applicants' own disclosure, there was no reason to believe that individual membranes could be fixed to the end of an open chamber through the use of a frictionally engaged ring only. This result is particularly surprising given the small dimensions of Applicants' fixing ring.

Applicants submit that their application is now in condition for allowance, and favorable reconsideration of their application in light of the above amendments and remarks is respectfully requested. Allowance of claims 1-3 and 5-17 at an early date is earnestly solicited.

The examiner is hereby authorized to charge any fees associated with this Amendment to Deposit Account No. 02-2958. A duplicate copy of this sheet is enclosed.

Respectfully submitted,



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